Remarks

Applicants appreciate the Examiner's acknowledgment that claims 2, 3, 7, 8, 12, 13, and 23 appear to be free of the prior art of record.

The Amendments

New claims 74-83 replace claim 27. The recitations of 70%, 75%, 90%, 96%, and 98% identical and the equation defining T_m are supported at page 14, line 22 to page 15, line 2:

> Typically, for stringent hybridization conditions a combination of temperature and salt concentration should be chosen that is approximately 12-20°C below the calculated T_m of the hybrid under study. The T_m of a hybrid between a transmembrane serine protease polynucleotide having a coding sequence disclosed herein and a polynucleotide sequence which is at least about 50, 55, 60, 65, 70, preferably about 75, 90, 96, or 98% identical to that nucleotide sequence can be calculated, for example, using the equation of Bolton and McCarthy, *Proc. Natl. Acad. Sci. U.S.A. 48*, 1390 (1962):
>
> $T_m = 81.5\ ^\circ C - 16.6(\log_{10}[Na^+]) + 0.41(\%G + C) - 0.63(\%formamide) - 600/l$),
>
> where l = the length of the hybrid in basepairs.

The specification has been amended to insert the ATCC Accession Number for plasmid pCR-TMSP3.

None of these amendments introduces new matter.

Objection to the Drawings

The drawings have been objected to under 37 C.F.R. § 1.84 or 1.152. Formal drawings of Figures 1-9 accompany this amendment. Withdrawal of this objection is respectfully requested.

Objection to the Specification

The specification has been objected to for containing blank spaces immediately following the description of the "ATCC Accession Number" for plasmid pCRII-TMSP3 on page 89, line 2. The specification has been amended to insert PTA-3433 in place of the blank spaces. Withdrawal of this objection is respectfully requested.

The Rejection of Claims 27 and 69-71 Under 35 U.S.C. § 112, second paragraph

Claims 27 and 69-71 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Claim 27 has been canceled, mooting its rejection. Applicants respectfully traverse the rejection of claims 69-71.

The Office Action asserts that the recitation of a "polynucleotide that hybridizes under stringent conditions" is unclear because the specification

> discloses in page 15, lines 3-5 that there is more than one stringent condition and discloses at least two substantially different wash conditions: 4X SSC at 65 C for stringent conditions and 0.2X SSC at 65 C for highly stringent conditions. Therefore, it is unclear as to which polynucleotides are being claimed since these wash conditions will result in different polynucleotides being hybridized to the polynucleotides recited in the claims.

Paper 11, page 3, line 20 to page 4, line 3. Amended claim 69 no longer includes the recitation "stringent hybridization conditions." Thus this rejection of claim 69 has been rendered moot. Applicants respectfully request its withdrawal.

To advance prosecution, claim 27 has been canceled and replaced with new claims 74-83. The indefiniteness rejection should not apply to these new claims. Claims 74 and 75 are the independent claims of the new claim set. Claims 74 and 75 define "stringent hybridization

conditions" by reciting a % identity between the probes of recitations (b) and (a) and by reciting that the stringent hybridization conditions are selected so that the T_m of a hybrid of (b) and at least 225 contiguous nucleotides of SEQ ID NO:11 or the cDNA insert of pCRII-TMSP3 is approximately 12-20°C below the T_m calculated according to the formula "$T_m = 81.5°C - 16.6(\log_{10}[Na^+]) + 0.41(\%G + C) - 0.63(\%formamide) - 600/l$, wherein l = the length of the hybrid in basepairs." The definition of "stringent hybridization conditions" recited in claims 74 and 75 is definite. Thus, the rejection should not apply to new claims 74-83.

The Rejection of Claims 27 and 69-71 Under 35 U.S.C. § 112, First Paragraph

Claims 27 and 69-71 stand rejected under 35 U.S.C. § 112, first paragraph as lacking adequate written description. The rejection is respectfully traversed.

The written description rejection of claims 27 and 69-71 is based on the recitation of polynucleotides that "hybridize under stringent conditions." This recitation has been deleted from independent claim 69. Claim 27 has been canceled. Thus, the rejection as it applies to claims 27 and 69-71 is rendered moot. Applicants respectfully request withdrawal of the rejection.

The rejection should also not be applied to new claims 74-83. The Office Action's rejection of claim 27 was based on the following:

> claim 27 is still directed to a genus of polynucleotides of any function comprising at least 225 nucleotides of a polynucleotide which can hybridize under any condition to the complete complement of the polynucleotide of SEQ ID NO:11 or the complete complement of the cDNA insert of plasmid pCRII-TMSP3.

Paper 11, page 5, lines 7-10, emphasis in original. First, the polynucleotide probes recited in new claims 74-83 do not encompass polynucleotides "of any function." The recited polynucleotide probes detect a coding sequence of a polypeptide. Thus, the recited probes have the function of being able to detect the recited coding sequence. Whether the recited probes do or do not have any other "function" is irrelevant and need not be described.

Second, new claims 74-83 specifically define stringent hybridization conditions. Claims 74 and 75 are the independent claims of the new claim set. Claims 74 and 75 recite that the stringent conditions are selected so that the probes of recitations (b) and (a) are at least 70% identical and recite that the stringent hybridization conditions are selected so that the T_m of a hybrid of (b) and at least 225 contiguous nucleotides of SEQ ID NO:11 or the cDNA insert of pCRII-TMSP3 is approximately 12-20°C below the T_m calculated according to the formula "$T_m = 81.5°C - 16.6(\log_{10}[Na^+]) + 0.41(\%G + C) - 0.63(\%formamide) - 600/l$, wherein l = the length of the hybrid in basepairs." The specification explicitly supports this recitation at page 14, line 22 to page 15, line 2.

Finally, the Office Action asserted that "the polynucleotides of claim 27 may contain none of the nucleotides of the complete complement of the polynucleotide of SEQ ID NO:11 or the cDNA insert of plasmid pCRII-TMSP3." (Paper 11, sentence bridging pages 5 and 6.) To clarify this point, new claims 74 and 75 recite polynucleotides that hybridize under stringent conditions along the full length of at least 225 contiguous nucleotides of the nucleotide sequence shown in SEQ ID NO:11 (claim 74) or of the cDNA insert of plasmid pCRII-TMSP3 (claim 75).

The specification adequately describes the subject matter of new claims 74-83. Thus the written description rejection should not be applied to these claims.

The Rejection of Claims 27 and 69-71 Under 35 U.S.C. § 112, First Paragraph

Claims 27 and 69-71 stand rejected under 35 U.S.C. § 112, first paragraph as not enabled. Claim 27 has been canceled. Applicants respectfully traverse the rejection of claims 69-71.

As with the written description rejection, the enablement rejection is based on the Office Action's objection to the recitation of stringent hybridization conditions. Specifically, the Office Action asserts that the specification does not enable:

> (1) polynucleotides of any function comprising 225 nucleotides of a polynucleotide comprising the nucleic acid of SEQ ID NO:11 or the cDNA insert of plasmid pCRII-TMSP3, or any polynucleotide which hybridize[s] under any condition to the polynucleotides above, or (2) polynucleotides of any function which can hybridize to the polynucleotide of SEQ ID NO:11 or the cDNA insert of plasmid pCRII-TMSP3.

Paper 11, page 6, lines 10-14. Independent claim 69 as amended does not contain these recitations. Claim 69 as amended recites only those polynucleotides that the Office Action acknowledges are enabled. See Paper 11, page 6, lines 8-9. Applicants respectfully request withdrawal of the rejection.

The enablement rejection also should not apply to new claims 74-83. Claims 74 and 75 are the only independent claims of the new claim set. First, claims 74 and 75 do not recite polynucleotides having "any function" as asserted in the Office Action. Claims 74 and 75 are directed to polynucleotide probes that detect a coding sequence. The specification enables this function. For example, the specification discloses that "[t]he presence of a polynucleotide sequence encoding a transmembrane serine protease polypeptide can be detected by DNA-DNA

or DNA-RNA hybridization or amplification using probes or fragments of polynucleotides encoding a transmembrane serine protease polypeptide." Page 24, lines 5-8.

Second, claims 74 and 75 do not recite polynucleotides that "hybridize under any condition." Claims 74 and 75 specifically recite that stringent conditions are selected so that the probes of recitations (b) and (a) are at least 70% identical and that the stringent hybridization conditions are selected so that the T_m of a hybrid of (b) and at least 225 contiguous nucleotides SEQ ID NO:11 or the cDNA insert of pCRII-TMSP3 is approximately 12-20°C below the T_m calculated according to the formula "$T_m = 81.5°C - 16.6(\log_{10}[Na^+]) + 0.41(\%G + C) - 0.63(\%\text{formamide}) - 600/l$, wherein l = the length of the hybrid in basepairs." One of skill in the art at the time the application was filed would have been able to identify stringent hybridization conditions within the scope of the claims merely by applying the recited formula. This formula and its application have been known in the art since 1962. See the specification at page 14, line 24 to page 15, line 5.

The specification, together with the knowledge in the art, enables new claims 74-83. Thus, the enablement rejection should not apply to these claims.

The Rejection of Claims 62-64 Under 35 U.S.C. § 112, First Paragraph

Claims 62-64 stand rejected under 35 U.S.C. § 112 first paragraph as not enabled. To advance prosecution claims 62-64 have been canceled.

The Rejection of Claims 1, 4-6, 9-11, 14, 15, 22, 24, 27, 62, 64, and 69-71 Under 35 U.S.C., First Paragraph

Claims 1, 4-6, 9-11, 14, 15, 22, 24, 27, 62, and 64 stand rejected under 35 U.S.C. § 112 first paragraph as not enabled. Claims 27, 62, and 64 have been canceled. Thus the rejection of these claims is rendered moot. Applicants respectfully traverse the rejection as it applies to claims 1, 4-6, 9-11, 14, 15, 22, 24, and 69-71.

The Office Action asserts that claims 1, 4-6, 9-11, 14, 15, 22, 24, 27, 62, 64, and 69-71 are not enabled because each of these claims recites a vector, pCRII-TMSP3, that has been deposited without an indication that it will be irrevocably and without restriction be released to the public upon issuance of a patent. A declaration of inventor Richard Gedrich accompanies this response. The declaration states that the deposit will be made publicly available upon issuance of a patent. Thus the vector of claims 1, 4-6, 9-11, 14, 15, 22, 24, 62, 64, and 69-71 is enabled.

Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 27 and 69-71 Under 35 U.S.C. § 102 (b)

Claims 27 and 69-71 stand rejected under 35 U.S.C. § 102 (b) as being anticipated by Hillier *et al.* (GenBank accession number R78581; "Hillier"). Claim 27 has been canceled. The rejection of claims 69-71 is respectfully traversed.

To reject a claim as anticipated each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). See also MPEP § 2131. Hillier does not meet this standard.

Claim 69 as amended recites an isolated polynucleotide. The polynucleotide is selected from the group consisting of (a) a polynucleotide encoding a protein that comprises the amino acid sequence of SEQ ID NO: 12, (b) a polynucleotide comprising the sequence of SEQ ID NO: 11, (c) a polynucleotide comprising a coding sequence of a cDNA contained within plasmid pCRII-TMSP3 (ATCC Accession No. PTA-3433), and (d) a polynucleotide encoding a protein that comprises the amino acid sequence encoded by the cDNA of plasmid pCRII-TMSP3 (ATCC Accession No. PTA-3433). As acknowledged in the Office Action, Hillier teaches none of the polynucleotides recited in amended claim 69. Applicants respectfully request withdrawal of the rejection of claims 69-71.

Hillier also does not anticipate the probes recited in new claims 74-83. Hillier teaches a 402-nucleotide cDNA. Only a 151-nucleotide portion of Hillier's cDNA shares identity with SEQ ID NO:11. The Office Action acknowledges that Hillier does not teach the polynucleotide of SEQ ID NO:11 or the cDNA insert of plasmid pCRII-TMSP3. Paper 11, page 12, lines 15-17. Because Hillier's cDNA is identical to only 151 contiguous nucleotides of SEQ ID NO:11, Hillier does not teach a polynucleotide comprising at least 225 contiguous nucleotides of the complete complement of SEQ ID NO:11 (claim 74) or the coding sequence of cDNA insert of pCRII-TMSP3 (claim 75). Thus, Hillier does not anticipate element (a) of either claim 74 or 75.

Similarly, Hillier does not teach the polynucleotide probes recited in element (b) of claims 74-83, of which claims 74 and 75 are the only independent claims. These polynucleotides hybridize under stringent conditions "along the full length of at least 225 contiguous nucleotides" of the nucleotide sequence as shown in SEQ ID NO:11 (claim 74) or the coding sequence of the cDNA insert of plasmid pCRII-TMSP3 (claim 75). If Hillier does not disclose

225 contiguous nucleotides of either SEQ ID NO:11 or the recited insert, it cannot teach a probe that is at least 70% identical (or 75, 90, 96, or 98% identical) to those sequences and that hybridizes to those sequences under the recited conditions.

Hillier does not teach each and every element recited in new claims 74-83. Thus Hillier does not anticipate these claims.

The Rejection of Claims 27 and 69-71 Under 35 U.S.C. § 102 (b)

Claims 27 and 69-71 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Paolini-Giacobino *et al.* (*Genomics*, *44*:309-320, 1997; EMBL accession number U75329, Swiss Prot accession number O15393; "Paolini-Giacobino"). Claim 27 has been canceled. Applicants respectfully traverse the rejection of claims 69-71.

Paolini-Giacobino is cited as teaching "several fragments which are complementary to the polynucleotide of SEQ ID NO:11." Paper 11, page 13, lines 13-14. The Office Action asserts that the disclosed fragments anticipate "a polynucleotide comprising at least 225 nucleotides of a polynucleotide which hybridizes to a nucleic acid comprising the complete complement of SEQ ID NO:11." Paper 11, page 13, lines 15-17.

Claim 69 as amended recites polynucleotides selected from the group consisting of (a) a polynucleotide encoding a protein that comprises the amino acid sequence of SEQ ID NO:12, (b) a polynucleotide comprising the sequence of SEQ ID NO:11, (c) a polynucleotide comprising a coding sequence of a cDNA contained within plasmid pCRII-TMSP3, and (d) a polynucleotide encoding a protein that comprises the amino acid sequence encoded by the cDNA of plasmid pCRII-TMSP3. As acknowledged in the Office Action, Paolini-Giacobino does not teach any of

these molecules. Paper 11, page 13, lines 10-12. Applicants respectfully request withdrawal of the rejection of claims 69-71.

Paolini-Giacobino also does not teach any of the polynucleotide probes recited in new claims 74-83. Paolini-Giacobino teaches a 492 amino acid sequence that is 24.6% identical to SEQ ID NO:12. The longest stretch of contiguous amino acid residues taught by Paolini-Giacobino that is identical to the amino acid sequence of SEQ ID NO:12 is 12 amino acid residues, encoded by 36 nucleotides. See the alignment provided with Paper 9. Thus Paolini-Giacobino cannot teach at least 225 contiguous nucleotides of the complete complement of the nucleotide sequence shown in SEQ ID NO:11 (claim 74) or at least 225 contiguous nucleotides of the complete complement of the coding sequence of the cDNA insert of plasmid pCRII-TMSP3 (claim 75).

Because Paolini-Giacobino teaches at most 36 contiguous nucleotides of SEQ ID NO:11, Paolini-Giacobino also does not teach a polynucleotide probe that hybridizes under stringent conditions along the full length of at least 225 contiguous nucleotides of the nucleotide sequence as shown in SEQ ID NO:11 (claim 74) or of the coding sequence of the cDNA insert of plasmid pCRII-TMSP3" (claim 75).

Moreover, the polynucleotides that hybridize under stringent conditions in recitations (b) of new claims 74 and 75 is also at least 70% identical to the complement of at least 225 contiguous nucleotides of SEQ ID NO:11 (claim 74) or of the complement of the coding sequence of the cDNA insert of plasmid pCRII-TMSP3 (claim 75). Paolini-Giacobino teaches a polypeptide that shares only 24.6% amino acid sequence identity with SEQ ID NO:12. Such a polypeptide cannot be encoded by a polynucleotide that is at least 70% identical (or 75, 90, 96,

or 98% identical) to any 225 contiguous nucleotides of SEQ ID NO:11 or of the cDNA insert of pCRII-TMSP3.

Paolini-Giacobino does not teach each and every element recited in new claims 74-83. Thus Paolini-Giacobino does not anticipate these claims.

The Rejection of Claims 27 and 69-71 Under 35 U.S.C. § 102 (a)

Claims 27 and 69-71 are rejected under 35 U.S.C. § 102 (a) as being anticipated by Kim *et al.* (*Biochim. Biophys. Acta 1518*:204-209; Accession number AB048796). Claim 27 has been canceled. Applicants respectfully traverse the rejection of claims 69-71.

Kim is cited as teaching a polynucleotide that is to identical to nucleotides 1-1672 of SEQ ID NO:11 except for one mismatch. Paper 11, page 14, lines 4-8.

Section 102(a) of 35 U.S.C. states that:

> A person shall be entitled to a patent unless---(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent.

The applicants for this patent, Yonghong Xiao and Richard Gedrich, conceived of the polynucleotides recited in claims 69-71 and in new claims 74-83 and reduced them to practice prior to the March 2001 date of the Kim publication. See the enclosed declaration under 37 C.F.R. §1.131.

Withdrawal of this rejection to claims 69-71 is respectfully requested.

Withdrawal of this rejection to claims 69-71 is respectfully requested.

Respectfully submitted,

Dated: June 10, 2003

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